Amino acids and proteins form the main building blocks for fetal and neonatal growth. Despite improvements in neonatal care, including postnatal nutrition, growth faltering and suboptimal outcome after premature birth are still frequently encountered. Nutrition can partly be held responsible. Over the years, there has been a trend in delivering amino acids earlier from birth onwards and in larger quantities. Studies showed positive results on efficacy, which was usually measured in terms of nitrogen balance (fig. 1) or stable isotope studies. Short-term safety has been questioned as parameters are difficult to interpret, while long-term effects are not frequently assessed. Besides, it is unlikely that we have achieved the optimal therapy with regard to protein supplementation for premature neonates yet.

It is therefore also important to gain insight into how the developing fetus is able to metabolize amino acids and proteins, and to translate this to preterm infants of similar gestational age. Exploring fetal metabolism and growth could enhance our understanding of the challenges of postnatal development, even though the placenta can no longer adjust and filter metabolites postnatally. Unfortunately, very little is known about fetal protein metabolism, which is also due to ethical and technical reasons. However, we hardly know how much nutrients the human fetus actually receives. Only a few studies have been performed using stable isotope techniques, which give us an indication of the uptake and metabolism of amino acids in human fetuses. These studies show that a relatively large proportion of amino acids taken up are utilized for oxidation rather than solely being used for protein synthesis [1, 2]. Extrapolation of the individual amino acid uptakes to total amino acid intakes (that could serve as a basis to determine total amino acid requirements of preterm infants of similar age) are hampered by the different metabolic fates of the individual amino acids. In addition, these studies do show that the
fetal liver is capable of synthesizing large quantities of albumin, possibly even higher than is currently seen in premature infants fed current recommended intakes [3]. Theoretically, it would thus seem to be possible to improve certain aspects of postnatal metabolism as well, as the metabolic apparatus of a premature infant should ontogenetically be able to achieve a high hepatic rate of protein synthesis under optimal circumstances (as in utero). Nevertheless, we must acknowledge the complex interplay between the placenta and the fetus [4].

![Fig. 1. Correlation plot of results in different trials investigating different amino acid intakes and nitrogen balances during the first few days of life of preterm infants. The size of the symbols resembles the number of infants included in the clinical trial.](image)
During the last decades, several studies have been performed in premature neonates on amino acid metabolism, mostly comparing different nutritional regimens in terms of protein content. Protein metabolism is, however, influenced by many other factors. For example, the quality (individual amino acid composition) of the intravenous solution or enteral formula or concomitant energy intake could influence the efficacy of protein handling and, therefore, the total requirements as well. Individual amino acid requirements during different stages of the postnatal course are, therefore, to be determined, of which only a start has been made. Besides, nonnutritional factors will influence the requirements and tolerability of amino acids, although these are hardly ever studied. Efforts should be undertaken to study the effects of intrauterine growth restriction, or needs during and following additional critical illnesses (besides prematurity itself) [5].

Thus, although we might attempt to determine amino acid requirements for the stable preterm infant based upon improved knowledge on both fetal and neonatal physiology, we are far from being able to predict the requirements for specific subgroups, such as being small for gestational age or stressed infants with additional diseases. Unfortunately, only few of these factors have been unraveled. Only by gaining more knowledge on both fetal and neonatal physiology and disease, we should be able to optimize growth and functional outcome in premature infants.

References